REMARKS

Claims 1-11 are pending in the instant application. Claims 7-11 have been withdrawn from consideration by the Examiner and subsequently canceled with prejudice by Applicants herein. Claims 1-6 have been rejected. Claim 1 has been amended in accordance with teachings at page 5, lines 4-15. Claims 2 through 6 have been canceled. Thus, no new matter is added by this amendment. Reconsideration is respectfully requested in light of these amendments and the following remarks.

I. Finality of Restriction Requirement

Upon reconsideration of the Restriction Requirement mailed May 7, 2003 and arguments presented by Applicants on August 7, 2003, the Examiner has joined Groups I and II in the instant application. The Examiner has maintained and made final restriction of Groups III-V. Accordingly, in an earnest effort to advance the prosecution of this case, Applicants are canceling herein claims 7-11 of Groups III-V without prejudice. In light of the finality of this Restriction Requirement, Applicants reserve the right to file a divisional application to the canceled subject matter.

II. Amendment to Specification

In accordance with the Examiner's request, Applicants have amended the first line of the specification to indicate all applications to which the instant application claims priority.

III. Rejection of Claims 1-6 under 35 U.S.C. § 112, second paragraph

Claims 1-6 have been rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In particular, the Examiner suggests that claims 1-6 are indefinite for reciting "measuring the levels of CC2 in cells, tissues or bodily fluids in a patient" because the exact meaning of the phrase and the source of the samples is not clear. The Examiner has also questioned the meaning and/or source of normal samples.

Accordingly, in an earnest effort to advance the prosecution of this case, Applicants have amended the claim to clarify that the cells, tissues or bodily fluids are **from** the patient.

Further, with respect to queries regarding a normal sample, Applicants respectfully direct the Examiner to page 9, line 30

through page 10, line 2 wherein normal samples are specifically defined. MPEP § 2173 is quite clear; definiteness of claim language must be analyzed, not in a vacuum, but in light of:

(A) The content of the particular application disclosure;

(B) The teachings of the prior art; and

(C) The claim interpretation that would be given by one possessing the ordinary level of skill in that pertinent art at the time the invention was made. The content of the application in this case makes clear what is meant by the phrase normal control, thus meeting the requirements of 35 U.S.C. § 112, second paragraph.

Claims 1 and 6 are also suggested to be indefinite for reciting "wherein a change in measured levels of CC2" because the exact meaning of the phrase, e.g. increased or decreased in the cancerous vs. normal sample, is not clear.

Accordingly, in an earnest effort to advance the prosecution of this case, Applicants have amended claim 1 to state that an increase in measured levels of CC2 in said patient versus normal human control is associated with the presence of cancer of the stomach or small intestine. Support for this amendment is provided in the specification at page 5, lines 4-15.

Withdrawal of these rejections under 35 U.S.C. § 112, second

paragraph is therefore respectfully requested.

IV. Rejection of Claims 1-5 under 35 U.S.C. § 112, first paragraph - Written Description

Claims 1-5 have been rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement. The Examiner has acknowledged the specification to disclose CC2 as a nucleic acid sequence of SEQ ID NO:1 which encodes the polypeptide of SEQ ID NO:2. However, the Examiner suggests that there are no other structures or structural features disclosed for any other CC2 molecules.

Accordingly, in an earnest effort to meet the prosecution of this case, Applicants have amended the claims to be drawn to a CC2 comprising SEQ ID NO: 1 or 2.

Withdrawal of this rejection under 35 U.S.C. § 112, first paragraph is therefore respectfully requested.

V. Rejection of Claims 1-6 under 35 U.S.C. § 112, first paragraph - Lack of Enablement

Claims 1-6 have been rejected under 35 U.S.C. § 112, first paragraph as failing to comply with the enablement requirement. The Examiner suggests that it would require undue experimentation for the skilled artisan to practice this invention because there

is no support in the specification for the enablement of the broadly claimed invention.

Applicants respectfully traverse this rejection.

As acknowledged by the Examiner, the specification discloses that CC2 is differentially expressed in stomach, colon and small intestine cancer samples. The small number of cancer tissue samples examined showing lower expression levels do not undermine these teachings. As shown in Table 2 beginning at page 19 of the instant application and taught at page 22 of the instant application, 75% of the stomach cancer samples tested and 50% of the small intestine cancer samples tested showed increased expression of CC2 as compared to control samples. Thus, the sensitivity of this marker is actually greater than many useful cancer therapeutics and diagnostics that have been FDA approved and are commercially available. For example, Genentech's product Herceptin and its diagnostic counterpart, the HercepTest are very successful commercially. Yet many publications show the relevant gene, HER-2, is overexpressed in only 30% of breast cancer patients. Hence, the sensitivity of CC2 claimed in the instant application is clearly sufficient for predictable detection of cancer of the stomach and small intestine as claimed.

Further, while mRNA levels may not have correlated to protein expression for a handful of unrelated mRNAs and/or proteins, that is not the case for cancer markers similar to CC2. CC2 is part of a class of proteins referred as Regenerating Proteins. CC2 is known as Regenerating Protein IV or REGIV. Applicants are providing herewith a recent article in Cancer by Yonemura et al. confirming protein expression of Regenerating Protein I or REGI as a diagnostic indicator of gastric cancer. This article is far more relevant to the instant invention and its predictability than those references cited by the Examiner. As shown by this reference, those of skill in the art have predictably used polypeptides similar to REGIV (CC2) in the claimed diagnostic setting in accordance with the teachings of the instant application without undue experimentation. Accordingly, there is no reason to doubt teachings of the instant specification regarding diagnostic utility of the CC2 polypeptide.

Finally, with respect to the Examiner's comments regarding enablement of staging or diagnosing metastases using the instant invention, while Applicants respectfully disagree with the Examiner, in an earnest effort to advance the prosecution of this case, Applicants have deleted these claims.

Thus, the remaining claim in this case is drawn to a method for detecting the presence of cancer of the stomach or small intestine in a patient by measuring levels of SEQ ID NO:1 or 2 in cells, tissues or bodily fluids from the patient. MPEP § 2164.04 is quite clear; a specification disclosure which contains a teaching of the manner and process of making and using an invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented must be taken as being in compliance with the enablement requirement of 35 U.S.C. § 112, first paragraph, unless there is a reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support. Methods for detecting SEQ ID NO:1 or 2 in a sample of cells, tissues or bodily fluid are clearly set forth in the specification at pages 11 through 14. Further, data evidencing use of CC2 as a diagnostic marker for stomach cancer and cancer of the small intestine is provided in the Examples section beginning at page 16 of the instant specification. Thus, the instant specification clearly teaches one of skill how to make and use the invention commensurate in scope with the claims.

Citation by the Examiner of references such as Tockman and Tascilar provides no reasonable basis for doubting the truth of

the instant application in providing a method for detecting cancer of the stomach and small intestine via measurement of CC2 as neither is related to CC2 itself. Further, these references clearly both support the value and utility of molecular markers as diagnostics in cancer. While cautions are set forth in these references regarding clinical application and the need to confirm results in the various samples through further experimentation, the MPEP and the courts have been quite clear:

> Usefulness in patent law, and in particular in the context of pharmaceutical inventions necessarily includes the expectation of further research and development. The stage at which an invention in this field becomes useful is well before it is ready to be administered to humans. See MPEP § 2107.01.

Further, there is nothing in the teachings of these references suggestive of such confirmatory experiments being considered undue by those skilled in the art.

Accordingly, the instant specification, which provides teachings of how to make and use the instant invention commensurate in scope with the claims meets the enablement requirements of 35 U.S.C. § 112, first paragraph. Withdrawal of this rejection is therefore respectfully requested.

VI. Conclusion

Applicants believe that the foregoing comprises a full and

complete response to the Office Action of record.

Accordingly, favorable reconsideration and subsequent allowance of the pending claims is earnestly solicited.

Respectfully submitted,

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